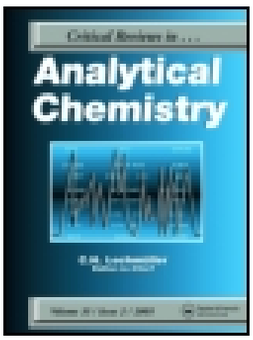

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# Flow analysis: A novel approach for classification

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# Flow analysis: A novel approach for classification

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**Abstract**

We have suggested a novel approach for classification of flow methods according to the conditions under which the mass transfer processes and chemical reactions take place in the flow mode: *dispersion-convection flow methods (1)* and *forced-convection flow methods (2)*. The first group includes continuous flow analysis, flow injection analysis, all injection analysis, sequential injection analysis, sequential injection chromatography, cross injection analysis, multicommutated flow analysis, multisyringe flow injection analysis, multi-pumping flow systems, loop flow analysis and simultaneous injection effective mixing flow analysis. The second group includes segmented flow analysis, zone fluidics, flow batch analysis, sequential injection analysis with a mixing chamber, stepwise injection analysis and multicommutated stepwise injection analysis. The offered classification allows to systematize a large number of the flow methods. Recent development and application of dispersion-convection flow methods and forced-convection flow methods are presented.

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**Keywords**

Flow analysis, classification of flow methods, automation, miniaturization

**Abbreviation**

AIA – All injection analysis

BI – Bead-injection

CFA – Continuous flow analysis

CIA – Cross injection analysis

DCFM – Dispersion-convection flow methods

FCFM – Forced-convection flow methods

FBA – Flow batch analysis

FIA – Flow injection analysis

LAV – Lab-at-valve

LFA – Loop flow analysis

LOV – Lab-on-valve

MC – Mixing coil

MCh – Mixing chamber

MCFA – Multicommutated flow analysis system

MCSWIA – Multicommutated stepwise injection analysis

MPFS – Multi-pumping flow system

MSFIA – Multisyringe flow injection analysis

SFA – Segmented flow analysis



 

SIA – Sequential injection analysis

SIA MCh – Sequential injection analysis with a mixing chamber

SIC – Sequential injection chromatography

SIEMA – Simultaneous injection effective mixing flow analysis

SWIA – Stepwise injection analysis

ZF – Zone fluidics



 

## 1. Introduction

There is a tendency of automation of chemical analysis due to the necessity to carry out a large number of analyses of environmental, food, pharmaceuticals and chemical industrial samples. Another current tendency is a miniaturization of analytical systems since it allows reducing the sample and reagent consumption and waste generation. In this matter the flow methods have been recognized as universal tool for automation and miniaturization of various analytical procedures.

Flow methods have been invented in the second half of the 20$^{th}$ century [1-6] and have become an attractive field for researchers in automation of chemical analysis. Initially flow methods were focused on automation of liquid samples analysis, but later it became possible to automate gaseous [7, 8] and solid samples [9]. Herewith, the flow methods allow to automate the main stages of chemical analysis: sampling, sample pre-treatment (separation, derivatization et al.), measurement of the analytical signal. To automate the chemical analysis the flow systems usually include pumps, valves, commutative tubes, mixing/reaction devises and detectors. A sequence of all analytical procedures is often controlled by a computer or a microprocessor.

The flow methods are well described in quite numerous monographs [10-13] and reviews [14-17] where their main fundamental principles and applications are presented. The evolution of the flow methods has been discussed from different points of view such as historical aspects [18], the commutation concept [19], the effect on analytical methodologies [16] and towards the development of Green analytical chemistry [17].

In the early 21st century, almost simultaneously several groups of scientists have paid attention to the possibility of carrying out the analytical procedures in the special mixing chambers. The aim of the researchers was to provide the automation of chemical analysis with high sensitivity and versatility of the flow manifold.

At the present time the numerous flow methods have been developed. It has been previously suggested to divide flow methods into two groups [20]: *flow analysis with continuous sampling* and *flow analysis with intermittent sampling*, where sample portions are injected into the system from a sampling loop. The main criterion for the classification of these methods is the type of sample injection into the flow system. Nevertheless, this classification does not consider the processes occurring in the flow manifold.

We have suggested the classification of the flow methods, which is based on the conditions under which the mass transfer processes and chemical reactions take place in the flow mode. The offered classification will allow to systematize a large number of the flow methods and to discuss their general advantages and disadvantages.



## 2. Classification

The conditions under which the mass transfer processes and chemical reactions take place in the flow mode may be used as the main criteria for dividing of all flow methods into two groups (Fig. 1): *dispersion-convection flow methods (1)* and *forced-convection flow methods (2)*.

The concept of the first group assumes the delivering of sample zone in the laminar flow of a carrier to a detector. The two mass transfer phenomena primarily responsible for the transportation of samples through dispersion-convection flow systems are convection and

diffusion. They both affect the broadening of the sample zone, which is referred to as sample dispersion in analogy with both chromatography and chemical reaction engineering [21]. Herewith, on the one hand, the diffusion provides mixing of the sample with reagents, but on the other hand, it leads to the dispersion of the sample in the flow of a carrier. It should be pointed out, that generally the equilibrium of the chemical reaction, which is usually used in the DCFM, is not achieved during the moving of the sample zone in the commutative tubes to the flow detector, what causes the reduction of the sensitivity of analysis. In this case, the analytical signal is formed by convection under a laminar flow regime and diffusion phenomena.

The concept of the second group assumes the mixing of the sample and reagents under forced convection, which provides high efficiency of the mixing and elimination of the dispersion. This flow-batch approach was first used in a flow technique [22] and it is frequently called as flow-batch mode. This group of methods is characterized by the involving special MCh into the flow manifold, where the solution of samples and reagents are delivered.

Moreover, it is possible to achieve the equilibrium of the chemical reaction proceeding in the MCh. Unlike DCFM the analytical signal in FCFM is formed by forced convection under a turbulent regime.

The forms of the analytical signals obtained by using the DCFM and FCFM are presented in Fig. 1. The analytical signal in case of FCFM is the difference between the detector signals corresponding to the sample solution and the background, like the signals measured in manual techniques [23]. The analytical signal measured by using DCFM is an asymmetric peak [12], which is less than the maximum achieved by FCFM due to the FCFM provide complete mixing of sample and reagent solutions in the MCh.

Moreover, in case of DCFM the dispersion of the sample depends on several parameters such as sample volume, flow rate, length and diameter of the commutative tubes, configuration of the mixing coils and detector design [12]. The dispersion of the sample in the DCFM leads to the decrease of sensitivity in comparing with manual procedures. However, such reduction of the sensitivity is not observed in case of FCFM. This possibility was demonstrated on the determination of epinephrine in pharmaceuticals [24].



## 3. Dispersion-convection flow methods

### 3.1. *The concept and capabilities*

The first invented flow method was the continuous flow analysis (Fig. 2 a) [25]. The principal concept of CFA assumes the continuous analysis of liquid samples. Mixing of the sample with reagents solutions in the CFA is carried out in the reaction/mixing coils under the convection and diffusion and the analytical signal of sample is continuously measured. The CFA has been widely used in analytical practice for on-line analysis [26, 27]. But its main disadvantage is the significant consumption of reagents and respectively large volume of waste generation.

Another flow method which is included to the DCFM is the flow injection analysis (Fig. 2 b) [28, 29]. The principal concept of FIA assumes the periodic injection of discrete portions of sample into a continuous laminar and non-segmented flow of carrier by using the valve. Mixing of sample and reagents' zones is occurred in the MC under the influence of diffusion and convection. To achieve high reproducibility strictly constant values of flow rate as well as the diameter of the coils and commutative tubes are used. Mostly the equilibrium of the reaction is

not achieved. It leads to the sensitivity reduction. The stopped-flow mode can be used to increase sensitivity especially for kinetic methods [30].

The FIA systems exploiting reagent injection in a sample stream allow to reduce the volume of reagent solution significantly. This strategy was demonstrated at the molybdenum blue method and reagent consumption was reduced by up to 240-fold in comparison to FIA with sample injection into a carrier [31].

Another approach for reducing volumes of reagents was reported in [32]. The authors have developed a novel flow injection technique, called as an all injection analysis, where all reagent solutions are injected into a reaction coil and all solutions are circulated for a fixed time. By this circulating process, the amount of the reagents' consumption is extremely eliminated.

Cyclic FIA allows to realize others approaches to minimize reagent consumption. This opportunity has been shown in cyclic flow-injection spectrophotometric determination of lead (II) based on its reaction with Arsenazo III [33]. A cation-exchange resin AmberliteJRA-120 was included after the detection cell for regeneration of Arsenazo III. After analyte determination, the lead (II) was retained in the column and the released reagent was directed back to its original reservoir. Similar approaches can be used to determine other anions.

Nevertheless, the common drawback of FIA like as CFA and AIA is the necessity to redesign manifold for each analyte analysis.

The first versatile flow manifold was realized in sequential injection analysis (Fig. 2 c) [34]. The SIA manifold includes a multi-way valve, a holding coil, a syringe or/and peristaltic pump, a reaction coil and a flow detector. The SIA concept assumes the sequential delivery of portions of a carrier, a sample and reagent solution into the holding coil. After switching of the

valve and reversing of the pump the sample and reagent solutions are moved through the reaction coil to the detector. In this case, a concentration gradient is formed, which leads to the partially overlapping of sample and reagent zones, forming an area where the reaction product is generated. Efficiency of the sample and reagent zones overlapping influences on the analytical signal and depends on the physical parameters of the system (the injected sample volume, the flow rate, the length and diameter of tubes in a manifold, the configuration and volume of the holding and reaction coils, the detector design) and solution properties (viscosity, molecular diffusion coefficients) [35]. SIA compared to CFA and FIA allows to reduce the reagent consumption and waste generation significantly. In this respect, the most progressive implementation of SIA has become the SIA «Lab-on-valve» (SIA LOV) [36-38], which assumes the performing analysis in the channels of multi-way valve. The SIA LOV is attractive from the viewpoint of minimizing the sample volumes, especially for the analysis of biological samples [39] and expensive reagents consuming [40]. Later a simpler approach, SIA with lab-at-valve (LAV) concept, has been proposed [41-48]. It is employed by attaching a device integrating sample processing and detection units on a port of a multiposition selection valve. This makes the SIA LAV simpler than the SIA LOV. The SIA LAV unit can be built using an ordinary and less precise machine tool, to have suitable functions for chemistries of interest and with a nut that can plug in a port of the valve in the usual way.

The sequential injection chromatography [49-52] should be also included to the DCFM. The SIC involves the combination of liquid chromatography and sequential injection analysis. Sample solution and eluent by means of syringe pump and a switching valve are sequentially aspirated through a chromatographic column included into the SIC manifold (Fig. 2 d). The SIC

can be realized in reversed-phase mode [53]. The monolithic chromatographic columns with a high porosity are used in SIC. They allow providing high efficiency of analytes separation at low back pressure (2.5 MPa) which is produced in flow systems. The monolithic columns consist of a single piece of high-purity polymeric silica gel rod with a bimodal pore structure: mesopores (average size 13 nm) used for separation and macropores (average size 2 μm) used for mobile phase flowing. In the above mentioned review [49] capabilities of SIC and high performance liquid chromatography were compared. The main advantages of the SIC are the significant reduction of the reagents' consumption and the equipment cost. Furthermore, it becomes possible to perform the derivatization in the automated mode.

The idea of DCFM is also implemented in multicommutated flow analysis system [54-58], simultaneous injection-effective mixing analysis [59, 60], multi-pumping flow system [61-64], multisyringe flow injection analysis [65-68], loop flow analysis [69] and cross injection analysis [70] methods. These methods are characterized by high reduction of sample and reagents consumption in compared with CFA, FIA, AIA and even SIA.

The multicommutated flow analysis system (Fig. 3 a) consists of a peristaltic pump and a set of solenoid valves, by means of which the required portions of reagents and sample solutions are injected into a carrier flow. The location of valves and configuration of all communications depend on an automated technique. Elimination of overheating of valves is an important aspect in the operation of MCFA. If the valve is switched ON for a long time, the heating takes place and deformation of polytetrafluoroethylene channels of the valves is observed. This problem is solved by the installation of special protective electronic systems [12].

The simultaneous injection-effective mixing analysis [59, 60] is a hybrid format of FIA, SIA and MCFA. Sample and reagent solutions are aspirated into the several holding coils through the solenoid valves by a syringe pump (Fig. 3 b), and then the zones are simultaneously transferred in a carrier flow into a MC by reversed flow toward a detector. It leads to effective mixing and rapid detection.

The multi-pumping flow system (Fig. 3 c) includes a solenoid piston pumps operating in a pulse mode. The sample and reagents are injected into the flow system by means of pumps and then are mixed in the mixing coils. The efficiency of the sample and reagents zones mixing increases due to the pulsation of the piston pumps in MPFS. However, dispersion is not excluded. The great advantages of MPFS are the high throughput of analysis, flexibility, easy configuration, and robustness.

The multisyringe flow injection analysis manifold (Fig. 4 a) includes special panel equipped with four syringes. Each syringe in the top has a three-way valve which directs the solution from syringe to the flow system or returns it back to the reagent reservoir to avoid the mixing of solutions from other syringe. The main advantages of MSFIA are the high robustness of the system due to the absence of pumping tubes; the possibility of using aggressive solvents and reagents due to inert materials of syringes; the possibility to commutate the flow system with sample pretreatment devices (e.g. filters, sorption columns) with the opportunity to use high pressure.

The loop flow analysis has been introduced for water analysis [69]. The main parts of LFA manifold (Fig. 4 b) are the multichannel peristaltic pumps, multi-way rotary valve and cross-shaped flow cell. The hermetic closed loop provides full protection against background

interference. Firstly, a sample is introduced into the sample loop using pump. Then, pump is kept working and pump is used to propel the reagents solution into the reagent loop and the spectrophotometer is set to zero. When the valve is switched, the sample and reagent are mixed and both pumps are stopped for the formation of the colored complex, which is monitored by using a detector. The LFA was used for shipboard applications in marine science and in on-line environmental monitoring applications.

The last suggested method of the first group is the cross injection analysis [70]. This method assumes that sample and regent solutions are injected perpendicularly into a carrier flow in a CIA cell (platform with cylindrical channels) by a peristaltic pump (Fig. 4 c). The mixing of the sample and reagent zones is carried out by their movement in a carrier flow from the CIA cell to the detector. The use of the CIA cell eliminates the need for valves using. Nevertheless, it does not provide the efficient mixing of the sample and reagent zones and the elimination of the dispersion.

3.2. *Recent development and application*

Nowadays, the DCFM are focused on the development of new automated sample preparation and multi-component methods and coupling of flow and separation methods (Table 1).

The liquid-liquid microextraction based on the DCFM has found wide application for sample preparation [71-73]. Several approaches have been developed: microcolumn phase separation [74], in-syringe approach [75] coupling with sequential injection system as well as magnetic stirring. The membrane methods of separation and preconcentration on the principles of DCFM such as pervaporation [76, 77] and gas diffusion [78-81] are also actively developed.

Moreover, the possibility of automation of single-drop headspace microextraction based on the SIA concept has been presented [82].

The bead-injection (BI) technique based on the principles of DCFM has used for sample preparation [83]. BI is the combination of the use of beads with a flowing stream of solution in a FIA/SIA system. Beads are utilized as solid surfaces to pre-concentrate or extract the analyte or to accommodate a chemical reaction. The flowing stream of solution is used to carry beads through the system. There is no need to regenerate the bead surfaces because they are discarded after each use and are replaced by fresh ones. It helps to reduce the risk of contamination, denaturation, and system clogging, and also, makes it possible to operate BI in the continuous flow system.

To increase the efficiency of SIA it was coupled with FIA [84]. Such coupling was implemented for the determination of lead (II) in water. The automated technique included the pre-concentration of the analyte in ion-exchange column operating in a sequential injection mode. After that, the elution of lead (II) was performed in flow injection mode for its subsequent spectrophotometric determination. Using such coupling flow system, it is possible not only to increase the sensitivity of lead (II) determination, but also to increase the sample throughput.

The effective implementation in DCFM is the coupling of the MSFIA and MPFS, which was applied for the determination of $^{226}$Ra in water samples [85]. Such flow system allows increasing the sample throughput and reducing the reagent consumption.

To realize multi-component DCFM several approaches have been proposed. The fist one means the simultaneous determination of several analytes provided by using of manifolds with several pumps, valves or detectors [86]. Additionally, the chemometric [87] and differential-

kinetic approaches [88] have been proposed and used in the multi-component flow analysis. The sample throughput of such systems is several times higher than conventional DCFM.

Recently attention was focused on coupling of DCFM with mass-spectrometry [89, 90], chromatography [91] and capillary electrophoresis [92-94] where the DCFM were used for automation of sample pretreatment. It was presented in the overview [94]. The benefits of hyphenated methods are high sensitivity and selectivity.



## 4. Forced convection flow methods

### 4.1. *The concept and capabilities*

The mixing under forced convection prevents the dispersion, that is common phenomenon in the methods of the first proposed group.

Mixing of the sample and reagents solution under forced convection is observed in the segmented flow analysis [95]. In SFA (Fig. 5 a) a continuous flow of the sample generated by a peristaltic pump is segmented by a gas bubbles and then mixed with the reagent flow in the mixing/reaction coils. The mixed flow is then moved to a flow detector, where the gas bubbles were preliminary removed. Sample segmentation by gas bubbles generates a turbulent flow, which leads to the homogenization of the reaction mixture. Furthermore, segmentation by the gas bubbles partially eliminates dispersion of the sample. SFA can be recognized as an intermediate approach between the flow methods of the first and the second groups.

The idea of forced convection has been better implemented in other FCFM: zone fluidics [96], flow batch analysis [23, 97-100], sequential injection analysis with a mixing chamber [101], stepwise injection analysis [102] and multicommutated stepwise injection analysis [103].

The last mentioned FCFM assume the main unit in the manifolds (Fig. 5 b-d, 6) – mixing chamber, where the portions of the samples and reagent solutions are sequentially delivered, mixed, thermostated (if necessary) and stored for a certain time to reach equilibrium.

Zone fluidics (Fig. 5 b) can be considered as a return to a SFA concept, but using the experience obtained in the SIA. ZF is defined as the precisely controlled physical, chemical, and fluid-dynamic manipulation of zones of miscible and immiscible fluids and suspended solids in narrow bore conduits to accomplish sample conditioning and chemical analysis. Fluids are propelled and manipulated in the manifold by means of a precise bi-directional flow pump. A holding coil between the pump and valve performs a similar role as in SIA. The ports of the multi-position valve are coupled to various reservoirs, reactors, unit operators, manifold devices, and detectors as indicated [96].

The mixing chamber in flow batch analysis is usually combined with a cell of the appropriate type of detector (Fig. 5 c). Portions of the sample and reagent solutions are sequentially delivered to the MCh by several peristaltic or solenoid pistol pumps. Mixing of the reaction solutions is carried out in the MCh with a magnetic stirrer or fishing line connected to an electromotor, then pause is kept to complete the reaction and finally the measurement of an analytical signal is performed [104]. Nevertheless, the FBA manifold has certain limitations. Thus, the involving of special devices for mixing of solutions in the MCh in FBA manifold complicates the design of the analyzer. The combination of the MCh with the detector cell limits the possibility of varying the sample volume and using of several types of detectors in one flow analyzer. The increasing of the optical path length for measuring the analytical signal in

spectrophotometric analysis is less possible. In FBA, the optical path length usually does not exceed 10 mm due to the limitations of inner volume of the MCh.

The manifold of sequential injection analysis with a mixing chamber (Fig. 5 d) differs from FBA in the conditions of the sample zone formation. Mixing of the sample with the reagent solutions is carried out in the MCh, and then the solution of the reaction product is injected into a carrier flow and delivered through the reaction coil to a flow detector. This manifold is most similar to SIA, but it eliminates the problem associated with an inefficient mixing of the sample zone and reagent solutions as it was in SIA.

The idea of forced convection mixing was implemented in the stepwise injection analysis. The SWIA manifold (Fig. 6 a) is similar to the FBA manifold. The SWIA manifold includes a multi-way valve, a reversible peristaltic pump, a flow detector and a thermostated MCh. But the SWIA manifold always includes gas delivering channel to mix the sample with the reagent solutions into the MCh by babbling, unlike the FBA manifold, where the solutions are mixed using the magnetic stirrer or fishing line connected to an electromotor. MCh can be implemented for the dissolution of solid-phase samples or solid-phase extraction of analytes from the sample [105-107] as well as for the absorption of gaseous analytes [108, 109]. The concept of SWIA assumes that all stages of routine analysis are strictly performed: sampling; sample preparation, including analyte pre-concentration (if necessary) or derivatization; analyte absorption into solution, when gases are analyzed; the dissolution, when solid samples are analyzed; the addition of reagent solutions to the sample solution; mixing solutions by a babbling; thermostating (if necessary); a pause for the formation of reaction product; and finally the measurement of the analytical signal.

The multicommutated stepwise injection analysis was proposed for automation of a multicomponent spectrophotometric analysis. The MCSWIA manifold includes two similar eight-way solenoid valves and two peristaltic single-channel pumps (Fig. 6 b). The first valve is used for sequential injection of samples, reagent solutions and a gas phase into the flow system. The gas phase is used for mixing of solutions in the mixing chambers, which are coupled with the second valve. The number of MCh is determined by the number of analytes and the corresponding number of colour-forming reactions, which are necessary for their determination. In turn, the number of MCh is limited by the number of ports of a valve.

4.2. *Recent development and application*

The FCFM have already found applications for the automation of analysis of aqueous samples [110-112], biological fluids [113], pharmaceuticals [114], biofuels [115, 116] and other samples (Table 2). It should be noted that the benefit of FCFM is the versatility of flow manifolds. The involving of the MCh into the flow manifold allows to automate various procedures of sample pretreatment (dilution, liquid-liquid extraction, gas absorption, dissolution of soluble solid-phase samples as well as the extraction of the analyte from the solid-phase samples et al.) rather easily.

Thus, the liquid-liquid extraction of analytes can be realized directly in the MCh for the pre-concentration [117]. In this case, the effective mixing of the aqueous and organic phases, as well as the phases separation, are carried out in the glass MCh. Sample, reagents and organic solvent are introduced into the MCh by a peristaltic pump using air as a carrier.

The ZF measurement of octanol-water partition coefficient of drugs [114] was developed. In this case, the system is consisted of a syringe pump with a selection valve, a holding column,

a silica capillary flow-cell and an in-line spectrophotometer. Exact microliter volumes of solvents (octanol and phosphate buffer saline) and a solution of the drug, sandwiched between air segments, were sequentially loaded into the vertically aligned holding column. The distribution of the drug between the aqueous and octanol phases was occurred by the oscillation movement of the syringe pump piston.

The SWIA has been implemented for the dispersive liquid-liquid microextraction. The dispersion of the extractant was also performed directly in the MCh. Such procedure was used for the fully automated preconcentration and spectrophotometric determination of antipyrine in saliva [118].

The idea of automation of headspace single-drop micro-extraction has been implemented based on SWIA [119]. The most important features of the SWIA with headspace single-drop micro-extraction are: automated determination of volatile compounds in complicated matrices including suspension; the successful coupling of the continuous operating process of headspace single-drop micro-extraction with the UV-VIS technique. The efficiency of the proposed system was successfully demonstrated in ammonia determination in concretes.

In case of gas analysis, the gaseous sample is delivered to the MCh, which is filled with the acceptor solution. During the absorption the gaseous analytes are conversed into the detectable forms. It was implemented in the SWIA determination of $H_2S$ [108] and mercaptans [120] in the natural gas; phenols [109] and nitrogen oxides [121] in the atmospheric air. The developed techniques do not require the use of standard gas mixtures for the calibration of the analyzer. Its calibration is carried out by the standard solutions in the acceptor stream, which are delivered to the flow detector.

To automate the soluble solid-phase samples analysis the ZF [96] and the SWIA were used and applied for the determination of biologically active substances in medicinal herbs [107]. The extraction of the biologically active substances from medicinal plants was carried out in the MCh under ultrasonication.

Moreover, FCFMs allow also carrying out the standard addition method [122-124]. Standard addition method was implemented in the flow-batch procedure for iron determination by atomic absorption spectroscopy in the hydrated ethanol fuel [125]. In the developed FB procedure the MCh was coupled with a nebulizer of the flame atomic absorption spectrometer by means of the valve. In this procedure the portions of a fuel sample, a standard solution of the iron (III) and deionized water were mixed in the MCh. Then, the mixed solution from the MCh by the valve was delivered into the nebulizer of the flame atomic absorption spectrometer. The injected amount of iron into the fuel sample was regulated by the ratio of standard solution and solvent.



**5. Conclusion**

The proposed overview has been presented a critical discussion of the possibility to classify the flow methods into two groups according to the conditions under which the mass transfer processes and chemical reactions take place in the flow mode: dispersion-convection flow methods and forced-convection flow methods.

All methods of the first group are characterized by a high throughput due to the reactions generally do not achieve the chemical equilibrium. The mass transfer processes and chemical reactions are carried out under the influence of the convection and diffusion. Nevertheless, the strict order of reagents and sample injection into the flow system allows to achieve the excellent repeatability. In general, the sensitivity in dispersion-convection flow methods is lower in

comparison with manual procedures. This decreasing of sensitivity is caused by two factors. In case of kinetically slow chemical reactions, continuous flow of carrier does not allow to optimize the condition of reaction products' formation (optimal time and the temperature of reaction media). Analysis in a stopped-flow mode only partially solves the first problem, since in this case the dispersion of the sample is increased.

The forced-convection flow methods provide highly sensitive measurements due to the physical and chemical equilibriums of the analytical process are achieved and the dispersion of the sample is excluded. Moreover, another benefit of forced-convection flow methods is the versatility of the flow manifolds. The involving of the mixing chambers in the flow manifolds makes it easy to automate such operations as dilution, standard additions injection, liquid-liquid extraction, gas absorption and dissolution of solid-phase samples. The main drawback of forced-convection flow methods is a low throughput due to time-consuming procedures of sequential aspiration of reagent and sample solution and their mixing in mixing chamber to achieve equilibrium.



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**Tables caption**



**Table 1. Applications of the dispersion-convection flow methods.**

| Flow method | Detection technique | Matrix | Analyte | On-line pre-treatment of sample | LOD | Sample throughput, $h^{-1}$ | Ref. |
|---|---|---|---|---|---|---|---|
| CFA | ASPM | river water | $Zn^{2+}$, $Cd^{2+}$, $Fe^{2+}$, $Cu^{2+}$, $Ni^{2+}$, $Co^{2+}$, Cr(VI) | - | 0.176-4.01 nM | - | 27 |
| FIA | FAAS | water | Cu | solidified floating organic drop microextraction | 0.58 ng $L^{-1}$ | 3 | 126 |
| FIA | CL | food | $SO_3^{2-}$ | pervaporation | 0.2 mg $L^{-1}$ | 30 | 127 |
| FIA | UV-Vis | saliva | acetaldehyde | gas-diffusion | 12.3 µg $L^{-1}$ | 9 | 128 |
| FIA | HPLS-UV | urine | opiate alkaloids biogenic amines | derivatization | 0.2-5 $10^{-7}$ M | - | 129 |
| MCFA | UV-Vis | honey | glucose | derivatization (immobilized glucose oxidase reactor) | 0.073 g $L^{-1}$ | 20 | 130 |
| MCFA | UV-Vis | water | $NH_4^+$, $PO_4^{3-}$ | - | 7 µg $L^{-}1$ $NH4^+$ 17 µg $L^{-1}$ $PO_4^{3-}$ | 56 | 131 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| MPFS | UV-Vis | water | Fe | oxidation | 0.15 mg $L^{-1}$ | 180 | 132 |
| MSFIA | UV-Vis | water | anionic surfactants | magnetic stirring-assisted dispersive liquid–liquid microextraction | 7 µg $L^{-1}$ | 10 | 133 |
| SIA | UV-Vis | saliva | $SCN^-$ | dispersive liquid-liquid microextraction | 0.017 mg $L^{-1}$ | - | 134 |
| SIA | ETAAS | water | Cu, Cd | dispersive liquid-liquid microextraction | 10 ngFe $L^{-1}$ 2 ngCd $L^{-1}$ | 10 | 135 |
| SIA | ETAAS | water | Cd | single-drop micro-extraction | 0.01 µg $L^{-1}$ | 6 | 82 |
| SIA | UV-Vis and BP-ANN | water | carbamate pesticides | - | 0.2-0.4 mg $L^{-1}$ | 18 | 136 |
| SIA | Q-ICP-MS | urine | Rh, Pd, Pt | pre-concentration (Metalfix™ Chelamine™ resin) | 0.4-1.2 ng $L^{-1}$ | 9 | 89 |
| SIA | CE-CD | water | $NH_4^+$, $K^+$, $Ca^{2+}$, $Na^+$, $Mg^{2+}$, $Mn^{2+}$, $Zn^{2+}$, $Cd^{2+}$, $Ba^{2+}$, $Cl^-$, $S_2O_3^{2-}$, $NO_3^-$, $SO_4^{2-}$, $NO_2^-$ | - | 0.3-2 µM | - | 137 |
| SIA | UV-Vis | drugs | Fe (II), ascorbic acid | - | 0.2 mg $L^{-1}$ Fe (II), 0.2 mg $L^{-1}$ ascorbic acid | 41 | 138 |
| SIC | UV-Vis | milk | melamine | dilution of the | 0.6 mg | 9 | 139 |

 

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | sample with sodiumdodecyl sulfate using a multiposition valve | $L^{-1}$ | | |

UV–Vis – spectrophotometry, ETAAS – electrothermal atomic absorption spectrometry, FAAS – Flame atomic absorption spectrometry, CL – chemiluminescence, BP-ANN – back-propagation-artificial neural network algorithms for multivariate quantitative analysis, Q-ICP-MS – quadrupole-inductively coupled plasma-mass spectrometry, CE-CD – capillary electrophoresis with contactless conductivity detection, HPLS-UV – High-performance liquid chromatography with UV-detection, ASPM – adsorptive stripping potentiometry.



 

**Table 2. Applications of the forced-convection flow methods.**

| Flow method | Detection technique | Matrix | Analyte | On-line pre-treatment of sample | LOD | Sample throughput, $h^{-1}$ | Ref. |
|---|---|---|---|---|---|---|---|
| SFA | UV-Vis | water and wastewater | $PO_4^{3-}$ | - | 4 µg $L^{-1}$ | 40 | 140 |
| FB | FAAS | hydrated ethanol fuel | Fe | standard-addition method | 0.04 mg $L^{-1}$ | 10 | 122 |
| FB | UV-Vis | water | $Cu^{2+}$ | liquid-liquid extraction | 5 µg $L^{-1}$ | 14 | 117 |
| FB | UV-Vis | biodiesel | glycerol | derivatization | 0.036 mg $L^{-1}$ | 14 | 115 |
| MCSWIA | UV-Vis | biodiesel | $Al^{3+}$, $Fe^{3+}$, Si, P | - | 0.3 mg $kg^{-1}$ $Al^{3+}$ 0.6 mg $kg^{-1}$ $Fe^{3+}$, Si, P | 6 | 116 |
| SIA-MC | PM | milk | $Cl^-$ | pseudo-titration | 0.1 mM | 17 | 141 |
| SIA-MC | UV-Vis | water | $PO_4^{3-}$ | standard-addition method | 0.024 mgP $L^{-1}$ | 324 | 124 |
| SIA-MC | UV-Vis | oil | $Fe^{3+}$ | dilution | 0.31 mg | 20 | 142 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | $L^{-1}$ | | |
| SWIA | UV-Vis | urine | $PO_4^{3-}$ | standard-addition method | 0.6 mg $L^{-1}$ | 10 | 123 |
| SWIA | UV-Vis | saliva | antipyrine | derivatization, dispersive liquid-liquid microextraction | 1 µM | 5 | 118 |
| SWIA | UV-Vis | natural gas | hydrogen sulfide | absorption | 20 µg $m^{-3}$ | 20 | 108 |
| SWIA | UV-Vis | medicinal plants | anthraquinones | ultrasound-assisted surfactant-mediated extraction | 4 mg $L^{-1}$ | 6 | 106 |
| SWIA | UV-Vis | concretes | $NH_4^+$ | headspace single-drop micro-extraction | 30 µg $kg^{-1}$ | 4 | 119 |
| ZF | UV-Vis | drugs | partition coefficient | liquid-liquid extraction | - | - | 114 |

UV–Vis – spectrophotometry, FAAS – Flame atomic absorption spectrometry, PM – potentiometry.



 

**Figures caption**

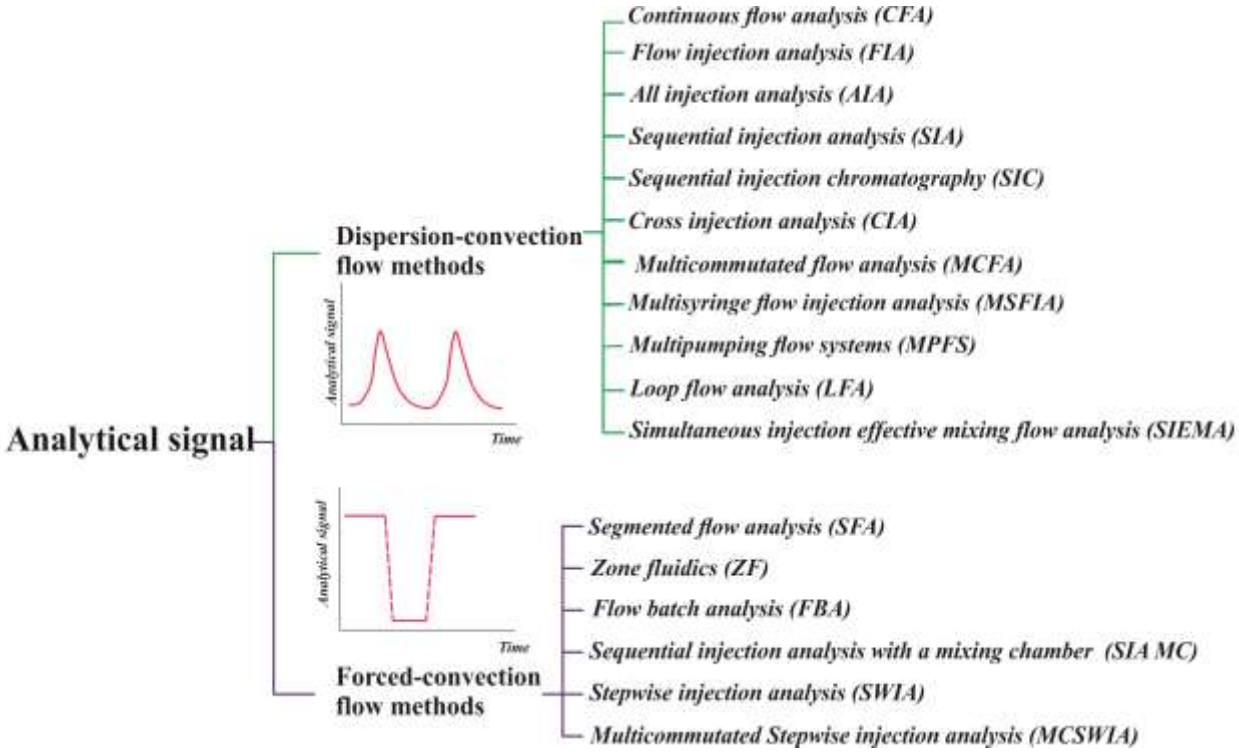


Fig. 1. Classification of the flow analytical methods based on the conditions under which the mass transfer processes and chemical reactions take place in the flow mode.

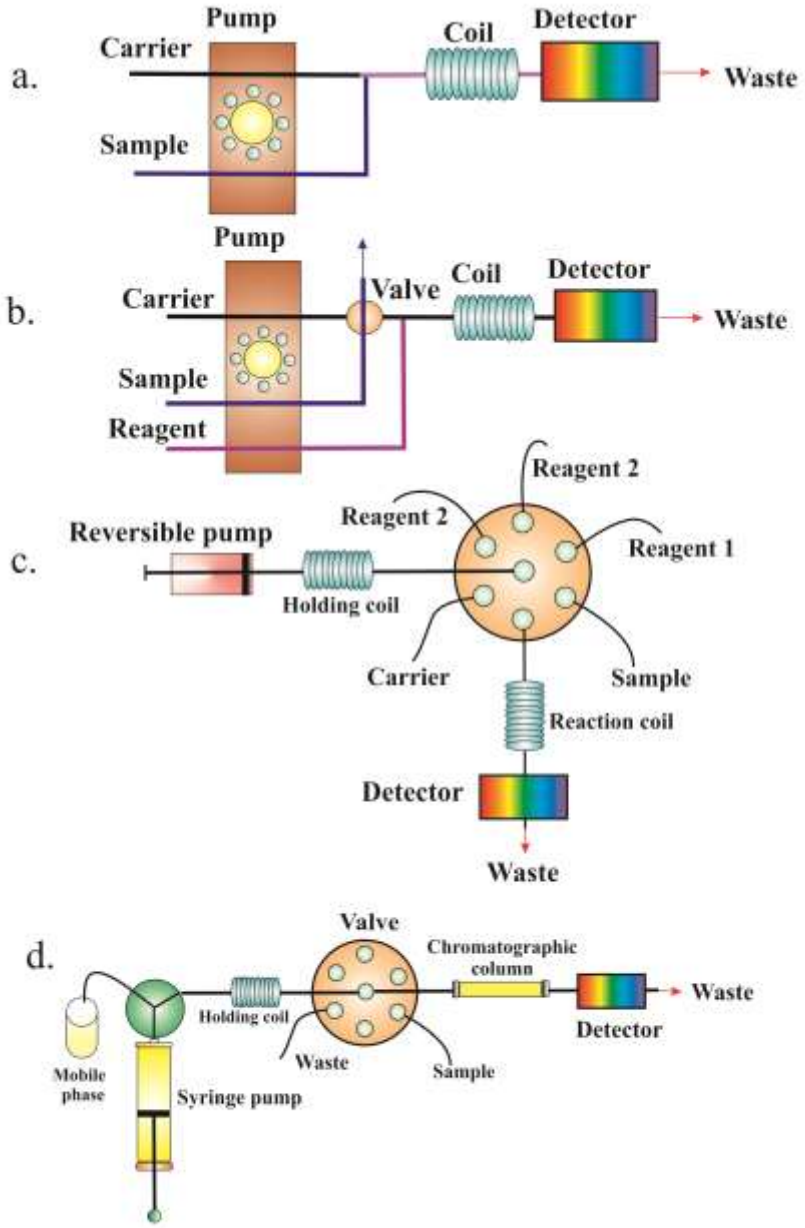


Fig. 2. The dispersion-convection flow methods: (a) CFA, (b) FIA, (c) SIA, (d) SIC

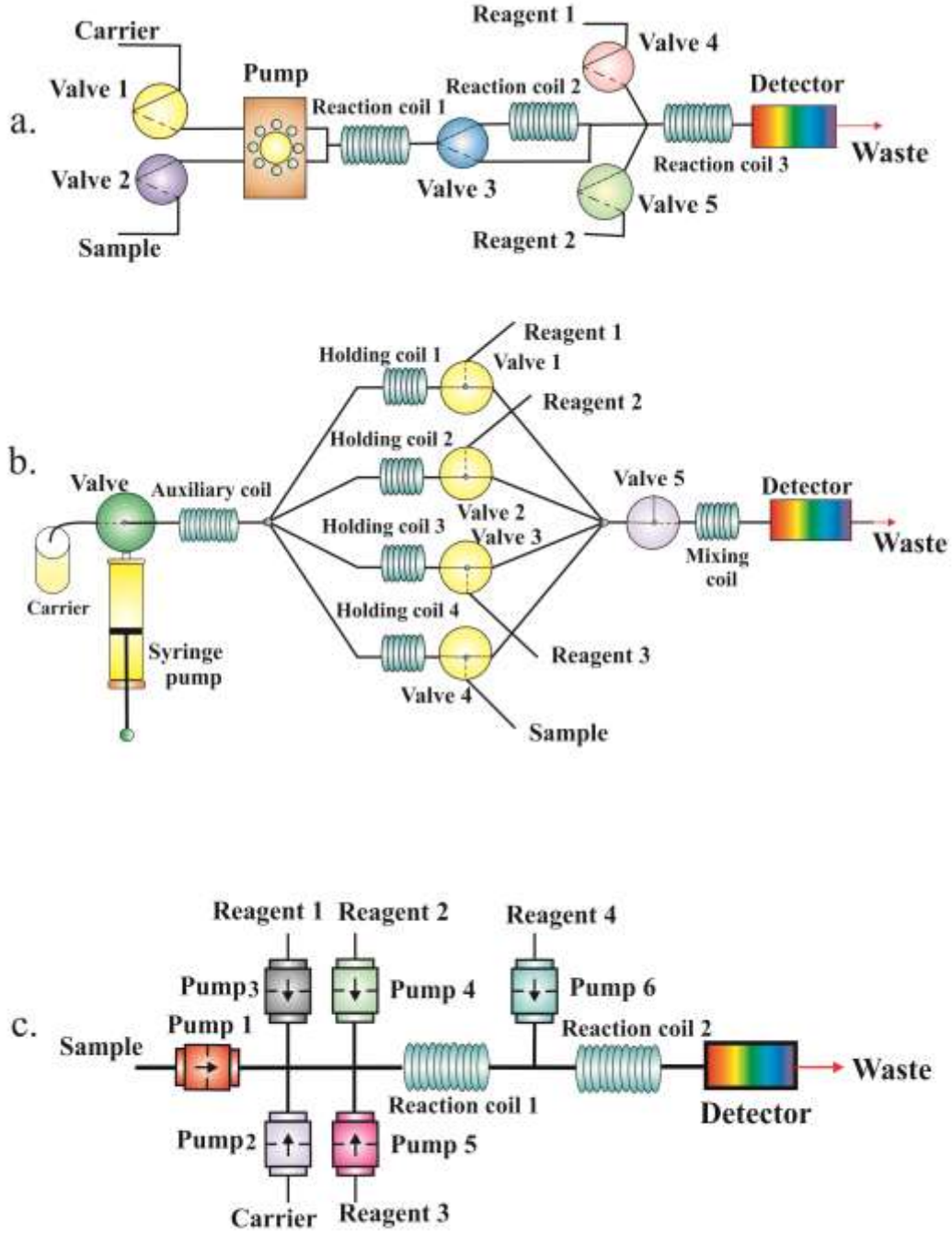


Fig. 3. The dispersion-convection flow methods: (a) MCFIA, (b) SIEMA, (c) MPFS.

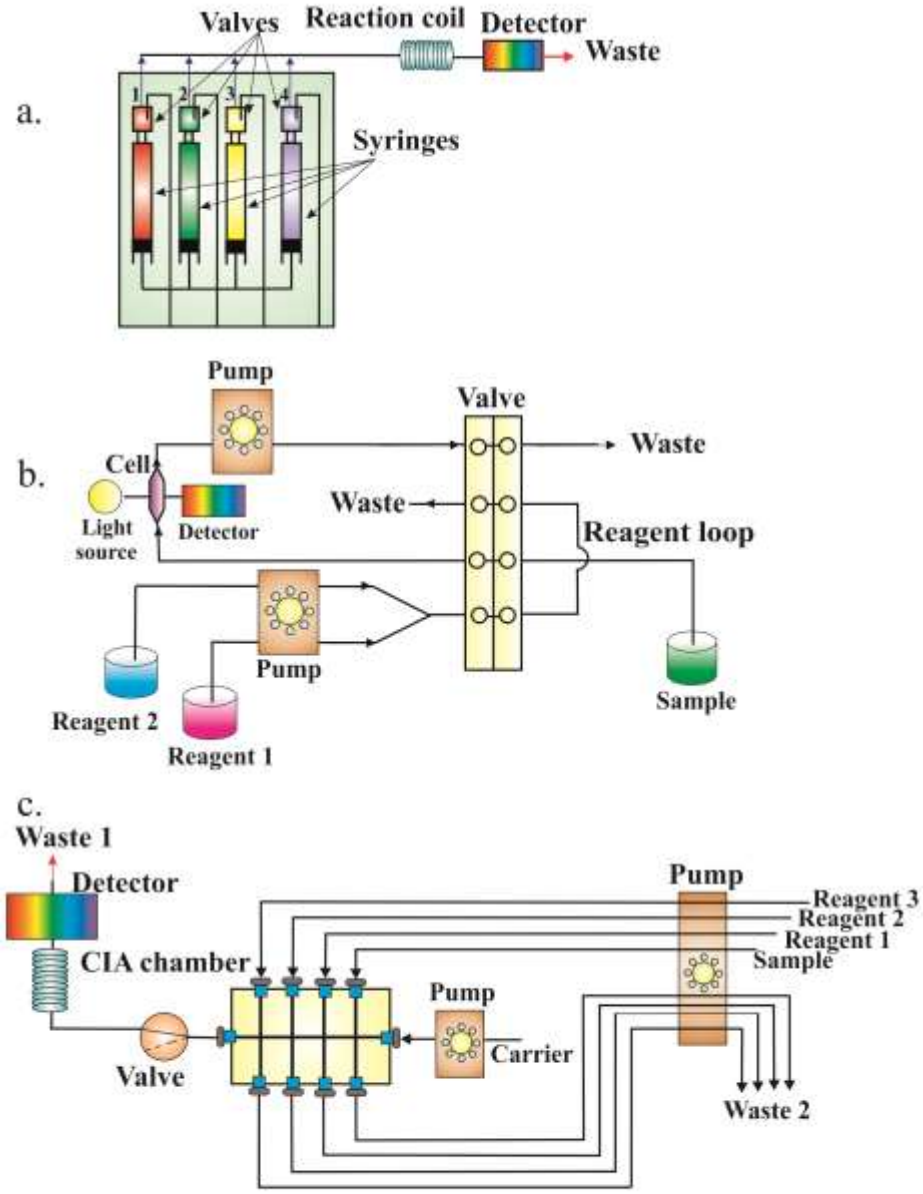


Fig. 4. The dispersion-convection flow methods: (a) MSFIA, (b) LFA, (c) CIA.

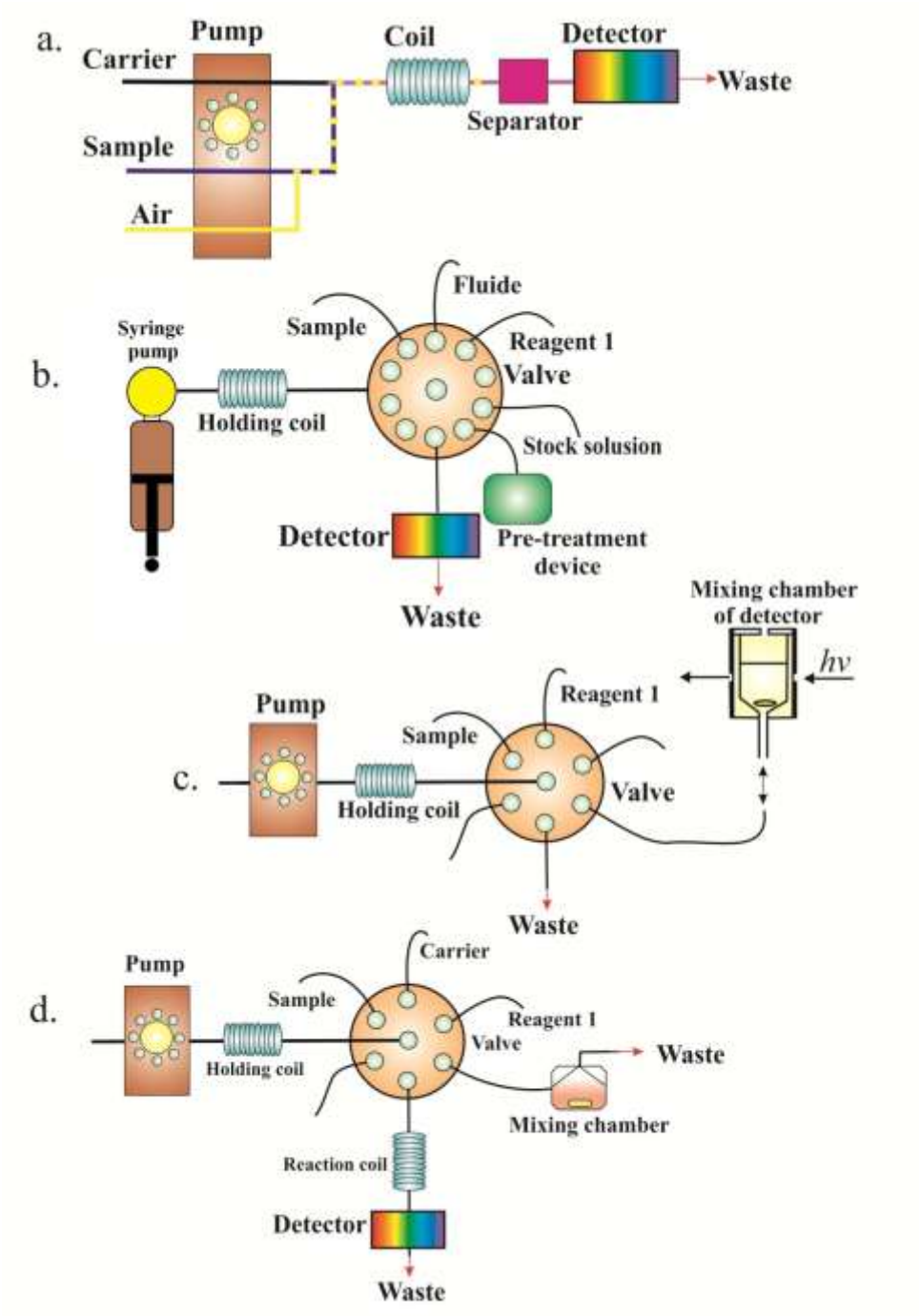


Fig. 5. The forced-convection flow methods: (a) SFA, (b) ZF, (c) FBA, (d) SIA MC.

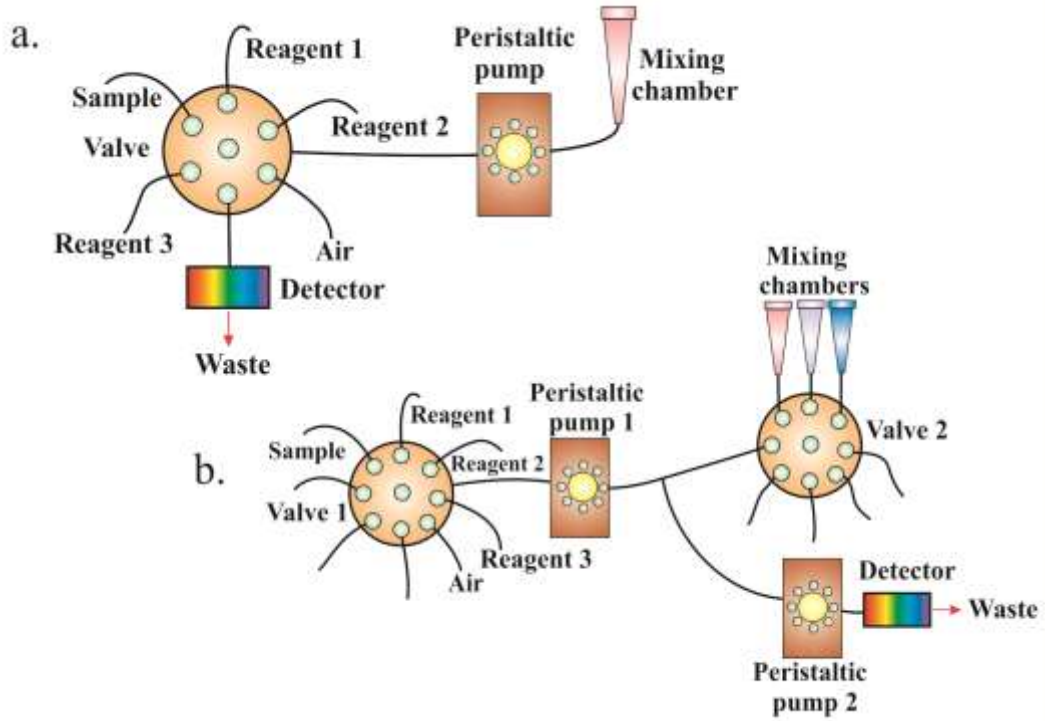


Fig. 6. The forced-convection flow methods: (a) SWIA, (b) MCSWIA.